REMARKS

In the Office Action mailed November 14, 2006, claims 1-27 were pending for consideration. All of the claims were rejected on various statutory grounds, each of which is addressed in turn below. Additionally, claims 3, 10 and 20 have been amended to language that more clearly indicates the intended claim limitations.

As such, by the present amendment, claims 3, 4, 10, 12, 14, 15, 20, and 27 have been amended. The Applicants submit that this amendment is not a narrowing amendment and that no new matter is added thereby. Accordingly, claims 1-27 remain pending in the present application. The Applicant respectfully submits that the present claims are allowable over the cited references.

Claim Objection:

Claim 27 was objected to because of a misspelling of the word "distearoyl." The claim has been amended to the correct spelling.

35 U.S.C. 112, Second Paragraph Rejections:

Claims 4, 14, 15, and 27 were rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite. Specifically, the Examiner has rejected claims 4 and 15 as indefinite because the metes and bounds of "cholesterol derivatives" and "fatty acid derivatives" are unclear. Claims 4 and 15 have been amended to delete the term "derivative." It should be noted that this amendment was made merely to move the prosecution forward, and should not be seen as being in agreement with the Examiner.

Additionally, claim 14 has been rejected as indefinite because the term "the covalent bond" allegedly lacks antecedent basis. Claims 12 and 14 have been amended to clarify the term "covalent bond."

Furthermore, claim 27 has been rejected due to allegedly unclear language. This claim has been amended to more clearly indicate the intended claim limitations. Reconsideration is respectfully requested.

35 U.S.C. § 102 Rejections:

The Examiner has rejected claims 1-4, 6, 7, 9, 12, 13, 15, and 17 under 35 U.S.C. § 102(b) as being allegedly anticipated by U.S. Patent No. 5,393,335 (hereinafter "Puckett"). Puckett teaches an aqueous starch-oil composition containing a lubricant consisting of reaction products of a mixture of C_2 to C_{18} fatty acids with a polyethylene imine having a molecular weight of from about 800 to about 50,000. (col. 3, lines 15-18). Thus Puckett appears to teach fatty acids associated directly with a PEI backbone.

Independent claim 1 of the present application contains limitations to, *inter alia*, a lipopolymer comprising a lipid covalently bonded to a PEI backbone via a biocompatible hydrophilic polymer spacer. Pucket does not teach or suggest the use of such a spacer to covalently link a lipid to a PEI backbone, but rather the reference teaches the reaction products of fatty acids and PEI. The Applicants respectfully disagree with the arguments provided by the Examiner that Puckett teaches a lubricant having the same physical structure as claimed in the present claims. The presence of a biocompatible hydrophilic polymer spacer in the lipopolymers of the present claims is one of the significant differences between the physical structures of the

Puckett lubricants and the lipopolymers of the present claims. Such a spacer increases the distance between the lipid and the PEI backbone, thus altering the physical and chemical properties of the lipopolymer. Accordingly, Puckett does not teach or suggest each and every element of claim 1, and as such, the Applicants respectfully request that these rejections be withdrawn. Additionally, because claims 2-4, 6, 7, and 9 depend from claim 1 and are considered to be narrower in scope, they will not be discussed in detail, and it is requested that these rejections be withdrawn as well.

Claim 12 of the present application contains limitations to, *inter alia*, a lipopolymer comprising PEI, a lipid, and a biocompatible hydrophilic polymer, where the lipid and the biocompatible hydrophilic polymer are covalently attached to the PEI backbone. Pucket does not teach the covalent attachment of both a lipid and a biocompatible hydrophilic polymer to a PEI backbone. It should be noted that the biocompatible hydrophilic polymer of the claim is a distinct element from the PEI backbone. The Examiner appears to be arguing that a portion of PEI can be considered to be the hydrophilic polymer. Assuming *arguendo* that such is the case, all of the elements of claim 12 have still not been taught or suggested by Puckett because the hydrophilic polymer would not be attached to the PEI backbone by a covalent bond. Please note that claim 12 has been amended to clarify that both the lipid and the hydrophilic polymer are linked to the PEI backbone by covalent bonds. As such, Puckett does not teach or suggest each and every element of claim 12, and it is respectfully requested that this rejection be withdrawn. Additionally, because claims 13, 15, and 17 depend from claim 12 and are considered to be narrower in scope, they will not be discussed in detail, and it is requested that these rejections be withdrawn as well.

35 U.S.C. § 103 Rejections:

The Cullis and Godbey References:

The Examiner has rejected claims 1-27 under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent No. 6,852,334 (hereinafter "Cullis") in view of J. Contr. Re. (1999) 60:149-160 (hereinafter "Godbey"). Cullis teaches polymer-lipid conjugates incorporated into a lipid bilayer of a liposome. (col. 12, lines 55-57). Such liposomes are fusogenic, and thus are intended to contact and fuse with a cell to release the enclosed contents of the vesicle. (col. 18, lines 47-55; col. 6, lines 9-14). Godbey teaches the use of PEI as a cationic DNA condensing agent that "will spontaneously adhere to and condense DNA to form toroidal complexes that are readily endocytosed by cells." (page 157, col. 2, first full paragraph).

The Examiner has indicated that it would be allegedly obvious for one of ordinary skill in the art to combine these two references and to thus utilize PEI as the polycation in the invention of Cullis. The Applicants respectfully disagree with this argument. PEIs are very soluble in water. Such solubility allows the formation of the toroidal complexes described by Godbey, which is a very different mechanism than that described in Cullis, namely encocytotic uptake of the solubilized toroidal complexes vs. the fusion of liposomes. As such, one of ordinary skill in the art would not have been motivated to combine these two references due to the disparate mechanisms of action taught by each reference. Additionally, one of ordinary skill in the art would not have had a likelihood of success in utilizing a PEI backbone in the liposomal structures of Cullis due to the high solubility of PEI and the difficulties inherent in forming the liposomes of Cullis. On page 157 of Godbey, it is stated that "while Oku et al. demonstrated disruption of phosphatidylserine liposomes by branched PEI, this effect was not seen to any great

degree when the liposomes were constructed from phosphatidyl choline/phosphatidyl serine." Such a statement further underscores the complicated and unreliable nature of PEI molecule incorporation with liposomes. As such, it would not be obvious to one of ordinary skill in the art to simply combine these references to arrive at the present claims. As such, the Applicants respectfully request that these rejections be withdrawn.

The Epand and Ogris References:

The Examiner has also rejected claims 12-21, 24 and 25 under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent No. 5,283,185 (hereinafter "Epand") in view of Gene Therapy (1999) 6:595-605 (hereinafter "Ogris"). Epand teaches the use of mixed lipid dispersions to facilitate the transfer of nucleic acids into cells (abstract). Epand is essentially teaching the use of liposomes in a similar manner to Cullis. Example XX states that none of the cationic cholesterol derivatives by themselves form stable homogenous dispersions by sonication, and it was necessary to add a phospholipid to form the mixed lipid dispersion. Such dispersions are micelles/liposomes as is indicated in Example XXIV, namely that at the optimal dispersion/DNA ratio, nearly all DNA were complexed with liposomes.

Ogris used PEGylation of pre-formed nanoparticles of a PEI/DNA complex that require sufficient stability during the PEGylation. This necessitates the use of the extremely large PEIs (800,000 Da) used by Ogris. Smaller PEIs would reversibly dissociate from Ogris-type PEGYlated nanoparticles during PEGylation, and thus would not be applicable to medium size and smaller PEIs. Ogris further states on page 595, that PEGylating PEI for complex formation is not used in order to prevent the undesired effects of PEG modified polycations on the DNA condensation process. Accordingly, one of ordinary skill in the art would not have been

motivated to combine these references. Additionally, there would have been no likelihood of success in such a modification due to the statements of Ogris that such a PEGylation process would interfere with the condensation process. Accordingly, it is requested that the rejections of claims 12-21, 24 and 25 be withdrawn.

The Epand and Godbey References:

The Examiner has also rejected claims 12-15, 17-21, 24, and 25 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Epand in view of Godbey. As Epand teaches liposomes similar to Cullis, as is discussed above, same arguments of the Cullis/Godbey combination apply to this situation. The mechanisms of action are very different between the products taught by Epand and those taught by Godbey, namely encocytotic uptake of the solubilized toroidal complexes vs. the fusion of liposomes. As such, one of ordinary skill in the art would not have been motivated to combine these two references due to the disparate mechanisms of action taught by each reference. As has been discussed, on page 157 of Godbey, it is stated that "while Oku et al. demonstrated disruption of phosphatidylserine liposomes by branched PEI, this effect was not seen to any great degree when the liposomes were constructed from phosphatidyl choline/phosphatidyl serine." Such a statement underscores the complicated and unreliable nature of PEI molecule incorporation with liposomes. As such, it would not be obvious to one of ordinary skill in the art to simply combine these references to arrive at the present claims. As such, the Applicants respectfully request that the rejections of claims 12-15, 17-21, 24, and 25 be withdrawn.

Accordingly, claims 1-27 remain pending in the present application. In view of the amendments and remarks herein, the Applicants respectfully submit that the present claims are

allowable over the cited references, and requests that the rejections be withdrawn and that the claims be allowed to issue.

CONCLUSION

In view of the foregoing, the Applicants assert that claims 1-27 of the present application present allowable subject matter and the allowance thereof is requested. If any impediment to the allowance of these claims remains after consideration of the present amendment and above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone Dr. Todd Alder, or in his absence, M. Wayne Western, so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 14th day of May, 2007.

Respectfully submitted,

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